Prof Nielsen concluded that the data from this 5-year follow-up of the MANTRA-PAF trial suggest that first-line treatment of AF with RFA led to improved outcomes with decreased occurrence and burden of symptomatic AF compared with patients who received AAD therapy. However, he acknowledged that there are currently no data that indicate RFA improves survival compared with AAD therapy, and the risk of severe complications associated with RFA must be considered when advising patients.

Education Program Fails to Improve Adherence to Apixaban: The AEGEAN Study

Written by Emma Hitt Nichols, PhD

The addition of an educational program to apixaban therapy did not improve patient adherence to therapy. Gilles Montalescot, MD, PhD, Pitié-Salpêtrière Hospital, Paris, France, presented data from the AEGEAN study [NCT01884350].

Vitamin K antagonists have multiple limitations, including regular laboratory monitoring to ensure that the INR is maintained within the narrow therapeutic window, frequent dose adjustments, multiple food and drug interactions, and the risk of bleeding [Mani H, Lindhoff-Last E. *Drug Des Devel Ther*. 2014]. In contrast, the novel (nonwarfarin) oral anticoagulants (NOACs) have fixed dosing, do not require laboratory monitoring, and have few food or drug interactions [Heidbuchel H et al. *Europace*. 2013]. However, patient adherence to NOAC therapy has been suboptimal because patients do not undergo frequent monitoring at an anticoagulation clinic. The purpose of the AEGEAN trial was to assess the efficacy of an education program in improving adherence to apixaban.

Adherence consists of 3 phases: (1) initiation, which occurs when the first dose is received, typically during hospitalization; (2) implementation, which refers to the patient's actual dosing relative to the prescribed dose; and (3) persistence, which is the time that a dose is omitted and no additional doses are taken.

In the open-label, phase 4 AEGEAN trial, patients with atrial fibrillation with a $CHADS_2$ score ≥1 were randomly assigned to receive apixaban with the standard of care or apixaban plus an educational program that consisted of an education booklet about atrial fibrillation and anticoagulation for stroke prevention, a key ring, a short message service alert via a mobile phone, a smartphone application, and access to a virtual clinic with staff from an existing anticoagulation clinic. The standard of care consisted of the usual information about apixaban treatment. After 24 weeks, patients who received the education program were randomly assigned to receive the standard of care or to continue the education program for an additional 24 weeks.

The primary end point was the effect of education on the implementation phase of adherence at 24 weeks. The secondary end points included the effect of education on the persistence phase of adherence at 24 weeks, the effect of an education program on efficacy and safety of apixaban, and identification of predictive risk factors for nonadherence. Patients were excluded if they were at a high risk of bleeding, could not self-administer apixaban, were hospitalized, or were in long-term residential care.

There was no significant difference in the implementation phase of adherence among the treatment arms at 24 weeks. Similarly, the rate of persistence at 24 weeks was 91.1% in the arm that received the education program compared with 90.5% in the standard-of-care arm. In addition, there was no significant difference in clinical outcomes at week 24 between the treatment arms.

In conclusion, Prof Montalescot stated that overall the data suggest that there is a high rate of adherence and persistence to apixaban during the first 6 months of therapy. However, the addition of an education program did not further improve adherence. The effect of the education program beyond 6 months will be evaluated in the second portion of the AEGEAN trial.

BELIEF Study: Left Atrial Appendage Ablation Improves Long-standing Persistent AF

Written by Emma Hitt Nichols, PhD

Empirical electrical isolation of the left atrial appendage (LAA) for the treatment of long-standing persistent (LSP) atrial fibrillation (AF) improved freedom from AF and atrial tachycardia (AT) without increasing complications compared with standard ablation. Luigi Di Biase, MD, PhD, Albert Einstein College of Medicine, Bronx, New York, USA, presented data from the BELIEF study [NCT01362738].

LSP AF is difficult to treat with catheter ablation [Tilz RR et al. *J Am Coll Cardiol*. 2012]. This is likely due to multiple origins of AF, including from the pulmonary vein and regions such as the superior vena cava, ligament of Marshall, coronary sinus, crista terminalis, left atrial posterior wall, and LAA [Di Biase L et al. *Circulation*. 2010]. The purpose of this study was to determine if the empirical electrical isolation of the LAA, in addition to pulmonary vein isolation and ablation of extrapulmonary triggers, would improve freedom from AF or AT.

The BELIEF trial was a randomized, open-label, parallel-group trial with 173 patients who had LSP AF that was

refractory to antiarrhythmic drugs. Patients were randomized to undergo empirical electrical isolation of the LAA plus standard ablation or standard ablation alone. The primary end point was recurrence of AF/AT lasting >30 seconds. The secondary end points were postablation heart failure or AF-related hospitalization, stroke, and mortality.

At baseline, the mean age was 64 years, 68% of patients had hypertension, and 20% had diabetes. The $CHADS_2$ score was 0 in 23.1% of patients, 1 in 35.3% of patients, and ≥2 in 41.7% of patients. The mean radiofrequency time was 93.1 and 77.4 minutes ($P<.001$) for the LAA and standard-of-care (SOC) arms, respectively. In the LAA arm, the LAA could not be isolated in 11 patients due to technical difficulty, and ablation was performed with only partial isolation. In the SOC arm, 9% of patients demonstrated sustained arrhythmia from the LAA and these patients were treated with LAA isolation.

Patients who underwent LAA isolation experienced a significantly greater single-procedure success rate (56%) compared with patients who underwent standard ablation (28%; HR, 1.92; 95% CI, 1.3 to 2.9; log-rank $P=.001$) at 12 months. The cumulative overall success was 76% in the LAA arm compared with 56% in the SOC arm (HR, 2.24; 95% CI, 1.3 to 3.8; log-rank $P=.003$).

At 6 months, all patients who received LAA isolation underwent transesophageal echocardiography (TEE). In 48 patients, low peak flow velocity defined as <0.4 m/s was detected, as well as 1 patient with a LAA thrombus and 1 patient with LAA smoke. Function was preserved in 48% of patients. There were no differences in AF and heart failure–related hospitalization in the LAA isolation arm compared with the SOC arm. There were no treatment-related deaths, and 4.5% of patients in the SOC arm experienced a stroke. There were no strokes or transient ischemic attacks in the LAA arm. Periprocedural complications included pericardial effusion (1 patient in each arm) and gastrointestinal bleeding (1 in the SOC arm).

Dr Di Biase concluded that the results of the BELIEF trial suggest that empirical electrical isolation of the LAA in patients with LSP AF improved freedom from AF/AT without increasing complications associated with treatment.

EAST-AF: Short-term AAD Therapy After Ablation Fails to Improve Long-term Outcomes

Written by Emma Hitt Nichols, PhD

Short-term treatment with an antiarrhythmic drug (AAD) in patients with atrial fibrillation (AF) who underwent catheter ablation reduced the recurrence of AF or atrial tachycardia (AT) at 90 days, but did not improve outcomes at 1 year. Kazuaki Kaitani, MD, Tenri Hospital, Nara, Japan, presented data from the EAST-AF trial [Kaitani K et al. *Eur Heart J*. 2015. In press; NCT01477983].

During the first several months following catheter ablation for the treatment of AF, transient AF or AT may occur, likely as a result of irritability associated with ablation. The purpose of the EAST-AF trial was to evaluate the role of short-term AAD use immediately following ablation for AF in improving long-term outcomes.

In the EAST-AF trial, 2044 patients were randomly assigned to receive AAD or be in the control group for 90 days. The primary end point was recurrent tachyarrhythmias at 1 year. The secondary end points included recurrent AT within the first 90 days, and adverse events. Recurrent AT was defined as an AF, atrial flutter, or AT event that lasted >30 seconds; need for repeat ablation; hospital admission; or need for a Vaughan Williams class I or III AAD.

At baseline, the mean age was 65.9 and 60.7 years in the AAD and control arms, respectively, and the duration of AF ranged from 24.7 to 26.1 months. Paroxysmal AF was present in 68.1% and 66.9% of patients, whereas persistent AF was present in 22%. The $CHADS_2$ score was ≤1 in 70.0% and 77.6% of patients, 2 in 18.9% and 15%, and ≥3 in 11.1% and 7.4%. The mean left ventricular ejection fraction was 64%.

At 1 year, 69.5% and 67.8% of patients in the AAD and control arms, respectively, were free from AF or AT (HR, 0.93; 95% CI, 0.79 to 1.09; $P=.38$). In addition, there was no significant difference in the primary end point among multiple prespecified subgroups, including age, sex, type of AF, left atrial dimension, and number of previously ineffective AADs. However, freedom from AF or AT was significantly greater in the AAD arm compared with the control arm at 90 days (59.0% vs 52.1%; log-rank $P=.001$).

The rates of all-cause mortality, ischemic stroke, intracranial hemorrhage, myocardial infarction, and heart failure hospitalization were <0.5% in both groups. Furthermore, there were no instances of cardiovascular death or systemic embolism in the AAD group (vs 0.1% in the control group). About 12% of patients in each group required cardioversion. Side effects related to the AAD occurred in 4.1% of patients and included bradycardia in 1.3% of patients.

Dr Kaitani acknowledged that this study was limited by lack of continuous electrocardiography monitoring and the differences in recommendations between Western AF management guidelines and the EAST-AF trial use of AADs.

Dr Kaitani concluded that, based on the data from the EAST-AF trial, short-term use of AADs in patients with AF who have undergone ablation did not result in improved outcomes at 1 year.